

response to prior conditioning with pharmacokinetic-targeted IV busulfan (130-145 mg/m²) and fludarabine (40 mg/m²) x 4 days (t-IV Bu/Flu) followed by HCT. All were treated with rituximab at 375 mg/m² on days 1 and 8 after a matched related (n = 7), mismatched related (n = 1), matched unrelated (n = 6), or mismatched unrelated (n = 2) HCT. Two patients received ATG as GVHD prophylaxis. Median time to neutrophil and platelet engraftment was 15 and 13 days, respectively. Maximum grades of aGVHD observed were 0 (n = 4), 1 (n = 7), 2 (n = 7), and 3 (n = 1). Moderate/severe cGVHD occurred in only 3/16. With a median F/U of 15 months (range: 2-33), complete response was achieved in 12, persistent residual disease in 3, and progressive disease in 1. CMV reactivation (n = 8), as well as bacterial (n = 8), fungal (n = 3), and viral (n = 3) infection did not appear to exceed historical rates without rituximab. After HCT, prolonged lymphopenia was demonstrated: Median absolute lymphocyte counts (0.84 K/uL) remained below the reference range through one year. In 5/16 subjects for which B-cell data was available, B-cell lymphopenia persisted to one year after HCT. The addition of rituximab 375 mg/m² to t-IV Bu/Flu followed by allogeneic HCT has encouraging activity in the treatment of lymphoid malignancies. While both absolute and B-cell lymphopenia were observed through one year after HCT, infectious complications have not exceeded historical rates.

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THE INCIDENCE OF HEPATIC SINUSOIDAL OBSTRUCTION SYNDROME (SOS) FOLLOWING A PREPARATIVE REGIMEN OF DOSE TARGETED INTRAVENOUS BUSULFAN AND CYTOXAN AND A GRAFT VERSUS HOST DISEASE PROPHYLACTIC REGIMEN OF TACROLIMUS AND METHOTREXATE: A SINGLE INSTITUTION EXPERIENCE

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Hepatic sinusoidal obstruction syndrome (SOS) is a common complication of preparative regimens in the setting of stem cell transplantation. The use of intravenous Busulfan (Bu), however, resulted in decrease in the incidence of SOS to 8%. The graft-versus-host-disease (GVHD) prophylactic regimen seems also to impact the risk of SOS following an ablative transplant. The goal of this study is to determine the incidence of clinically significant SOS in a homogenous cohort of patients who received an ablative regimen of dose targeted intravenous Busulfan and cytoxan (Bu/Cy), and received tacrolimus and methotrexate (Tac/MTX) for GVHD prophylaxis.

Methods: In this retrospective study, patients who received an ablative regimen of intravenous Bu/Cy, and received Tac/MTX for GVHD prophylaxis were identified. Data collected include: age, indication for transplant, disease status at transplant, stem cell source, date of transplant, date of onset of clinically significant SOS, and date and cause of death. Patients who underwent an ablative regimen of total body irradiation (TBI) and cytoxan and received the same GVHD prophylactic regimen were used for comparison.

Results: Between September, 2007 and August, 2009, 34 patients received an ablative regimen of intravenous Bu/Cy and GVHD prophylactic regimen of Tac/MTX. In this cohort, age ranged from 25 to 63 years old. Diagnoses were as follows: AML n = 20, MDS n = 7, CML n = 4, myelofibrosis n = 2, and NHL n = 1. Disease status at diagnosis was CR1 n = 16, ≥ CR2 n = 5, relapsed/refractory n = 2, untreated n = 6, PR n = 3, chronic phase CML n = 2. In this cohort, only three (8.8%) patients developed clinically significant SOS. Two patients were diagnosed within 3 weeks of transplant, however, one patient developed biopsy proven SOS 58 days post transplant. None of the patients in this cohort died of SOS. In 28 out of 34 patients, Bu pharmacokinetic (PK) studies were done properly. In two patients the Bu dose was increased and in one case the dose was decreased. In the comparison cohort, 29 patients received TBI/Cy conditioning regimen. In this cohort only one patient (3.4%) developed SOS.

Conclusion: The incidence of SOS in the cohort of patients who received dose targeted intravenous Bu/Cy and Tac/MTX for GVHD

prophylaxis was comparable to the reported incidence of SOS in literature and appears to be higher than the incidence of SOS in the TBI/Cy and Tac/MTX cohort.

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COMORBIDITY SCORE IN ALLOGENEIC MYELOABLATIVE TRANSPLANTS CONDITIONED WITH FLUDARABINE/I.V. BUSULFAN (FLUBU4)

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The assessment of comorbidity score was previously demonstrated to predict the risk of transplant related mortality (TRM) in patients undergoing standard myeloablative allogeneic hematopoietic stem cell transplantation (HSCT). Since Flu/Bu4 regimen has been associated with limited extra-hematologic toxicity, we analyzed whether the comorbidity score may still represent a useful tool in transplant patients conditioned with this regimen. Of 52 consecutive patients who received a matched HSCT with FluBu4 at our institution, 50 were evaluable for assessing their pre-transplant comorbidity score according to the initial description (Sorró M et al. Blood 2005, 106:2912). The total dose of I.V. Bu was 12.8 mg/kg in 18 patients while in the remaining patients a targeted dose was given (AUC: 4800 μM*min). Patients were divided in three groups: group A, score 0 (n = 8); group B, score 1-2 (n = 16); group C, score ≥ 3 (n = 26). The three groups did not differ significantly in age, diagnosis, previous lines of chemotherapy, type of donor and targeted vs standard dose of I.V. Bu. Patients with active acute leukemia at the time of HSCT were 12% in group A, 18% in group B and 29% in group C (p = ns). Thirteen patients (26%) died due to relapse of their malignancy and 11 (22%) due to transplant-related complications. TRM was 12% in group A, 37% in group B and 15% in group C despite the fact that the rate of acute GVHD grade II-IV was slightly higher in group C (34%), compared to groups A (12%) and B (31%). Patients in group C had a trend for higher relapse-related mortality, 38%, compared to 12% observed in each of the other groups (p = 0.07). After a median follow-up of 640 days (range: 111-2065), a greater number of patients were alive and in remission in group A (75%) (p = 0.04), compared to group B (50%) and C (34%). In conclusion, a higher comorbidity score correlated with worse overall survival largely due to increased relapse. However, it did not predict TRM in patients conditioned with FluBu4.

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CHILDREN WITH ACUTE LEUKEMIA: A COMPARISON OF OUTCOMES FROM ALLOGENEIC BLOOD STEM CELL AND BONE MARROW TRANSPLANTATION

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The relative merits of PBSCT versus BMT for children with standard and high risk hematologic malignancies remain unclear. In a retrospective single center study, we compared allogeneic peripheral blood stem cell transplantation (PBSCT) (n = 30) with bone marrow transplantation (BMT) (n = 110) in children with acute leukemia between January 1st, 2001 and September 30th, 2006. Four (13.3%) PBSCT patients received HLA identical sibling donors versus 38 (34.5%) who received marrow: 15 (50.0%) PBSCT recipients received HLA mismatched PBSC versus 10 (9.1%) receiving marrow. Nine (30.0%) PBSCT patients had an HLA matched unrelated donor versus 49 (44.5%) of marrow recipients. Two PBSCT (6.7%) were from mismatched unrelated donors versus 13 (11.8%) in the marrow recipients. The median age for PBSCT was 9 years versus 8 years for BMT. Descriptive statistics were used to summarize the demographic and medical variables. The unadjusted probabilities of disease-free survival were estimated using the Kaplan-Meier method. The association of graft-source and time to each of the study endpoints was estimated by Cox's regression model and the occurrence of GvHD was included as a time-dependent covariate. Time to both neutrophil engraftment and platelet independence